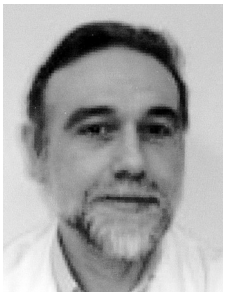
Editorial

The Diagnosis and Management of Patients with Giant Cell Arteritis



In most Western countries giant cell (temporal) arteritis (GCA) is the most common primary systemic vasculitis in later life[1,2]. However, controversies on diagnosis and management of patients with suspected GCA still exist.

In this issue of *The Journal,* Drehmer, *et al* analyzed data from a physician survey on diagnosis and management of GCA[3]. Two hundred and thirty-five respondents gave their opinions on crucial questions such as (1) decision to order temporal artery biopsy (TAB); (2) influence of previous corticosteroid therapy on TAB yield; (3) the need for contralateral biopsy; and (4) initial corticosteroid dose.

SHOULD TAB BE PERFORMED IN SUBJECTS WITH SUSPECTED GCA?

Patients with untreated GCA are more susceptible to blindness. This fact has contributed to general consensus among clinicians on the need for corticosteroid treatment in subjects with suspected GCA. Morbidity derived from TAB is minimal since it is performed by local anesthesia[4]. However, some physicians still consider biopsy unnecessary in some cases since it would not change treatment. In this regard, in a review of 135 TAB, Allsop and Gallagher reported 24 patients with normal biopsies who were treated because they were considered on clinical grounds to have GCA[5]. They suggested that TAB could be omitted and replaced by a trial of steroid therapy. According to them, biopsy should be reserved for patients with a strong medical contraindication to corticosteroids, or who fail to respond to treatment promptly. In contrast, investigators at the Mayo Clinic supported the need for biopsy[4,6]. They assessed the outcome of 134 residents of Olmsted County, MN who had undergone TAB in a 15-year period[6]. A 6-year median followup disclosed that only 8 of 88 with normal biopsy findings required corticosteroid therapy for GCA[6]. A more recent comparative analysis between patients with biopsy-proven GCA and biopsy-negative patients diagnosed with GCA according to previously proposed clinical criteria found that biopsy-proven GCA patients had more severe disease with a higher risk of severe ischemic complications and irreversible visual loss compared to biopsy-negative patients[7]. These observations suggest that TAB should be done before patients are committed to longterm corticosteroid therapy and highlight the prognostic value of TAB for defining a subset of patients with less severe GCA. Fortunately, most physicians who responded to the survey proposed by Drehmer, *et al* agreed on the necessity of performing TAB for suspected GCA[3].

WHO SHOULD UNDERGO TEMPORAL ARTERY BIOPSY?

The most important risk factor for having GCA is age. The incidence rate increases with age and peaks in patient groups over 70 years[1]. In the presence of elevated acute phase reactants, new features in elderly individuals, such as unexplained pain located above the neck, should prompt us to consider the possibility of GCA and the need for TAB[8]. Recent reports emphasize that GCA may present without clinically evident vascular involvement[9]. Some of these patients without overt vascular manifestations may present with fever of unknown origin[9]. Patients with silent GCA have lower hemoglobin values than other patients with GCA[10]. Isolated polymyalgia rheumatica (PMR) may also be a presenting manifestation of GCA[9]. In Lugo, Northwest Spain, TAB are usually considered in isolated PMR patients if they have constitutional syndrome and/or erythrocyte sedimentation rate (ESR) greater than 80 mm/h[11]. Following this protocol, we reported 8 (9%) positive TAB from a series of 89 patients with isolated PMR[11]. However, clinicians should not hesitate to perform TAB on individuals with clinical features of GCA and inappropriately low

See Diagnostic and management trends of giant cell arteritis, *page 1283 and* Temporal artery biopsy for giant cell arteritis, *page 1279*

ESR. Salvarani and Hunder identified 18 (11%) patients with GCA and pretreatment ESR less than 50 mm/h from a series of 167 patients with GCA[12].

All the evidence described above underlines the importance of a high degree of suspicion for GCA in Caucasians over the age of 60. In agreement with this conclusion, Elliot, *et al* performed a decision analysis for the management of GCA[13]. They concluded that due to the high cost of blindness, suspicion of disease must be very low before a physician can exclude performing a TAB[13].

DOES CORTICOSTEROID TREATMENT INFLUENCE TAB YIELD?

Many clinicians consider corticosteroid treatment for suspected GCA prior to TAB renders TAB meaningless. However, Achkar and coworkers confirmed the presence of histopathological findings of GCA in TAB of 9 patients who had received more than 15 mg/day of prednisone for more than 14 days before biopsy[14]. Although Achkar, *et al* did not prove that histologic features are unaffected by corticosteroids, they showed that the TAB positivity rate in this subgroup of patients was similar to that of untreated patients[14]. However, the proportion of positive specimens that yielded atypical histologic features of GCA in corticosteroid-treated patients, such as absence of giant cells or confinement of inflammation to the adventitia, was significantly higher than in untreated patients[14]. As a consequence, TAB should be performed soon after onset of treatment. Failing to do so within several days after the initiation of corticosteroid therapy should not be a reason for not performing TAB in patients with suspected GCA.

IS TAB SAMPLE SIZE IMPORTANT?

GCA affects vessels focally and segmentally, yielding areas of inflammatory vasculitic lesions juxtaposed with areas of normal artery. Klein, *et al* described isolated foci of arteritis (skip lesions) in 17 (28%) of 60 patients with GCA[15]. They also found small foci of arteritis in an otherwise normal biopsy specimen[15]. The length of TAB sample available for pathological study and examination of multiple histologic sections is therefore important for confirming pathological diagnosis of GCA. However, there is no unanimous consensus about the optimal length for biopsy[15-17]. To confirm suspected diagnosis of GCA, Kent and Thomas recommended a generous biopsy of about 5 cm in length of fresh vessel[16]. Large specimens, such as 4 to 6 cm, in patients in whom classic features of GCA are not well manifested were proposed by Hall and Hunder[4]. Nowadays, segments of at least 2.5 cm are considered acceptable for pathological review[7,11]. However, in a report also published in this issue of *The Journal*, Taylor-Gjevre and coworkers described that a threshold length of 1.0 cm of post-formalin fixed arterial segment was associated with increased diagnostic yield of GCA[17]. These authors recommended collecting a minimum TAB length of 1.5 cm to allow for tissue shrinkage during fixation that was estimated to be approximate 10%[17].

SHOULD WE PERFORM UNILATERAL OR BILATERAL TAB?

TAB should be done at the most symptomatic site[4,7]. A retrospective analysis showed that 14% of 234 patients were diagnosed with biopsy-proven GCA at the Mayo Clinic from 1976-1980 because TAB was performed on the other side[4]. As discussed by Drehmer, *et al*[3], more recent prospective studies support the need for proceeding with contralateral biopsy. In a prospective study on 200 patients with suspected GCA, Ponge, *et al* performed 200 bilateral TAB. They found 42 patients with positive TAB on at least one side. Interestingly, 4 patients with GCA would have been missed if only unilateral TAB had been performed[18]. These observations indicate that patients with high clinical suspicion of GCA and a negative biopsy on the most symptomatic side should undergo contralateral TAB.

WHAT ABOUT AN INITIAL DOSE OF CORTICOSTEROIDS?

General guidelines are needed although sometimes treatment must be individualized. A comprehensive review article emphasized that GCA requires an initial dose of prednisone of at least 40 to 60 mg as a single or a divided dose[19]. Other authorities recommend beginning with 40 to 60 mg/day of prednisone[2]. There is general agreement on the use of higher intravenous doses for patients who have experienced visual loss, e.g., methylprednisolone pulse therapy (1 g daily for 3 days)[2,10,19]. However, a large prospective clinical study is required to determine whether the efficacy of intravenous pulse methylprednisolone therapy may be better than high dosage oral prednisone to reduce the incidence of irreversible visual loss in patients presenting with recent visual ischemic manifestations.

A final point of controversy is whether corticosteroids should be given every other day or as a single or a divided daily dose. In a prospective randomized study Hunder, *et al* compared oral prednisone treatment in a divided dosage 3 times a day (15 mg/8 h) with a single daily dose of prednisone (45 mg) and prednisone every other morning (90 mg). After 1 month of treatment, they found a trend toward better disease control in the divided-dosage group compared to the single daily dose group, but no differences in the side effect profile between these 2 groups. However, in only 6 of the 20 patients receiving prednisone every other morning did the disease seem to be completely suppressed[20]. These results support the need for starting treatment with daily prednisone therapy in GCA.

In conclusion, accurate diagnosis and early onset of therapy are of central importance in the prevention of severe complications in GCA. Multicenter collaborative studies

should be implemented to establish consensus on the management of this important type of vasculitis.

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